

JOHN J. MEDINA

# **The Clock of Ages**

**Why we age – how  
we age – winding  
back the clock**



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## PART ONE

# *Who ages?*

## INTRODUCTION

Our first task in the beginning of this book is to attempt to define the process of aging. By the end, you will find this task will be mostly unaccomplished.

The reason for this ambiguity is manifold, and perhaps surprising. The problem is that there are so many ways to look at the roots of biological maturity. Some look to aging's final obligation, death, and attempt to work backwards from the event to describe what aging means. But even death can be difficult to define absolutely, in an it-makes-sense-to-the-biologist language. We will understand this ambiguity best by attempting a definition of our own. And we will do so in the same backwards style, first examining the process of death and then working our way in reverse.

### A working definition

At first blush, the inability to define death, and the body's prior preoccupation with survival, might sound odd. We have no ambiguities, for example, surrounding the material facts of such notable nonagenarians as the playwright George Bernard Shaw. Not only do we know when and how he expired (at the age of 94, after suffering a 108-degree fever), we have a general idea of what happened. He *died*, and from this event a corpse and a funeral were created.

And so it is for most of us. Death appears to be a definable, monolithic, biologically irreversible fact of life. Quibbling with its consistency seems a strange exercise, even an irrelevant one. We are forced, for better or worse, to link the words 'inexorable' and 'death' in a strong bond. Such a linkage is true, however, only if you don't look too closely.

Overarching definitions run into semantic and conceptual obstacles

quite easily. Automobiles and aunts both age, for example. But then, so do wine and cheese. We surely don't imply the same physical process – or outcome – is occurring in each. The only commonality is a certain time-dependent physical change, even a deterioration.

Because of this ambiguity, many researchers tether the process of aging to an event that appears more definable, at least to biological organisms. That event is 'natural causes'. Scientists think of aging in terms of probabilities, with mounting tenure increasing the likelihood of expiration. Aging, in their minds, is a decrease in the chance of survival. Death is a cessation of that decrease.

Though it leaves any explicit consideration of reproduction out of the picture, this definition of aging is not a bad start. Everything fated to have a beginning is also doomed to have an ending. We share, along with light bulbs and fan belts, an extinction so predictable that it almost appears planned. Focusing on death as the end point of this planned obsolescence gives a comforting linearity to our definition. But we deteriorate to what? 'Cessation of a decrease' has to *mean* something. Since all living things seem to undergo it, there must be some common thread to their experience of death. We ask a single question: Is there an overarching, universal definition of the biological process of death? This question lies at the heart of our ability to understand the aging process in biological life. It is the purpose of the chapters in this section to answer it.

To accomplish this task, we will first discuss the world of non-human biology, exploring the process of death in a variety of vertebrate and invertebrate organisms. Second, we will consider the mechanisms of human expiration, looking both biologically and historically for an explanation of our 'moment of death.' Finally, we will explore the evolutionary context of aging and death. By examining the force of natural selection on senescence, we will attempt to find a biological reason for its existence. Once a context is established, understanding the purpose may help us also understand the substance.

### A few ground rules

Several issues need clarifying before we begin. I will be using the terms 'aging' and 'senescence' interchangeably. This has its hazards, whether we consider multi-cellular organisms or simple single cells. Botanists, for example, use the term 'senescence' when they describe deciduous trees

shedding their leaves; that does not mean the tree is ‘aging’ in the traditional sense. Certain cells in our body undergo the process of senescence. This is a fairly well established series of specific internal biochemical events not necessarily leading to death, and not part of common definitions. Some cells age and die in living things – even in developing embryos – but leave the rest of the organism youthful and growing. It is important to distinguish between whole organismal aging processes and mechanisms occurring within individual cells. When considering evolutionary theory, we must distinguish between the forces exerted on an individual and those exerted on a group.

In addition to the terms ‘aging’ and ‘senescence’, I will soon be using words like ‘cells’ and ‘cell cycle.’ Although more formal definitions will follow as these pages unfold, I will give a brief description here. You remember from grade school that all human beings are composed of cells, those small, grease-lined objects that look like beach balls (Figure 1). A typical human has 60 trillion of these structures. Each cell has a nucleus, which is a glorified storage container for human genetic information. As you may recall, this information is locked up in structures called chromosomes, and is made of DNA.

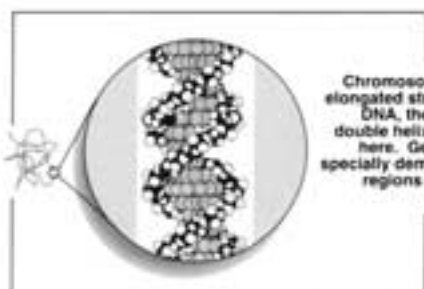
In order to keep us healthy, these cells must make copies of themselves. To do that, they simply copy their genetic information and then split in two. This process, a highly controlled and very complex event, is called mitosis (Figure 2). It is regulated for a critical reason, one that can be seen when the controls break down. If the cells start proliferating in an uncontrolled fashion, a tumor may be formed.

With that bit of biology under our belts, we can return to the subject of this chapter. We are going to analyze the notion of relevance and irreversibility of senescence in living things. Placing our own undeniable human mortality in the context of the natural world may increase our appreciation of life. And give us a firmer understanding of the inevitability of our own doom. We may discover if George Bernard Shaw was correct when he joked to a comrade about the nature of his epitaph.

I knew that if I hung around here long enough, something like this was bound to happen.

## Animal cell architecture

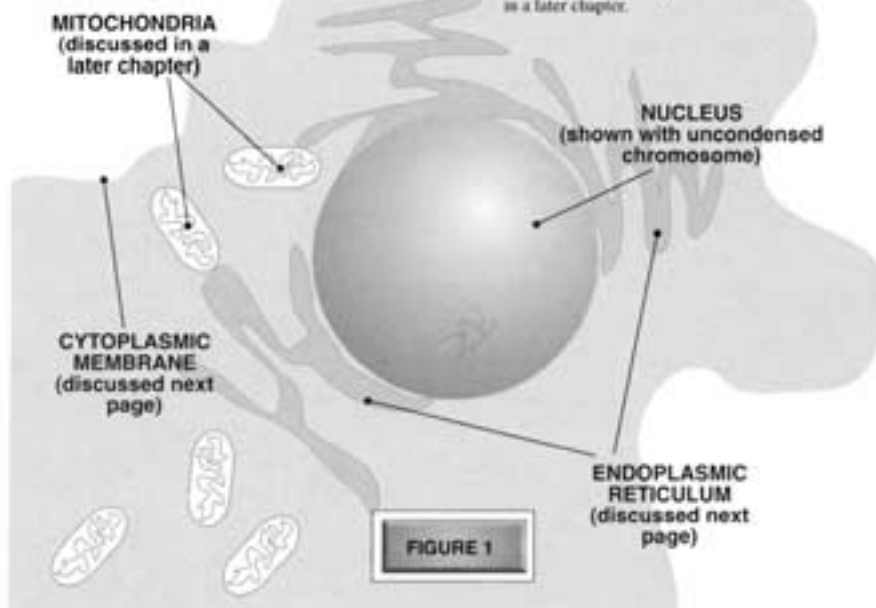
*A 'typical' animal cell, drawn below, looks something like a fried egg.*



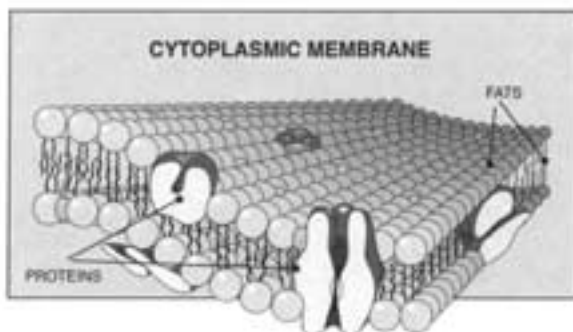
Chromosomes are elongated strands of DNA, the typical double helix shown here. Genes are specially demarcated regions of DNA.

THE 'YOLK' is termed the nucleus, the 'white' termed the cytoplasm. The nucleus is the command and control center for the cell. It contains the genetic information (housed in structures named chromosomes) necessary to run the day-to-day operations of the cell. Chromosomes are really long strands of DNA, the double helix pictured on the left.

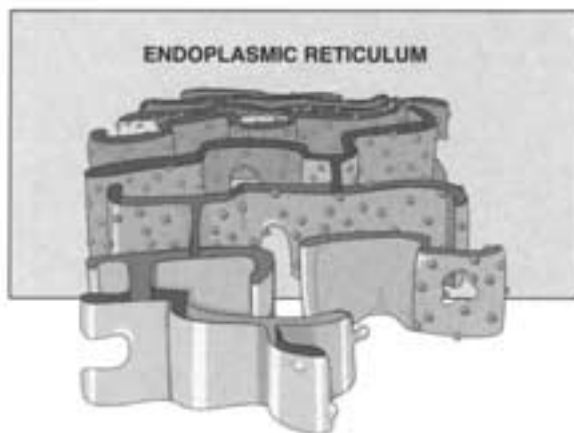
The cytoplasm has very few control functions. Instead, it contains the power supplies, manufacturing base, and much of the transportation infrastructure. In order to issue commands, the genetic information in the nucleus has to send out 'messages' to the cytoplasm, a topic we will consider in a later chapter.







The outer membrane is primarily composed of fats. Bobbing up and down in the membrane like a buoy are proteins. They often serve as 'receptors,' binding to external molecules and communicating the fact to the nucleus.



This tongue-twisting structure can be likened to an intracellular superhighway. The ER consists entirely of membrane-enclosed spaces. These spaces provide a network of conduits where various molecules can be transported.

